February 20, 2003

Edward W. Kordoski, MBA, Ph.D.
Executive Director
The Synthetic Organic Chemical Manufacturers Association (SOCMA)
U.S. Nitroglycerin Producers Consortium (USNPC)
1850 M. Street, N.W.
Suite 700
Washington, D.C. 20036

Dear Dr. Kordoski:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Nitroglycerin posted on the ChemRTK HPV Challenge Program Web site on October 29, 2002. I commend The Synthetic Organic Chemical Manufacturers Association (SOCMA) U.S. Nitroglycerin Producers Consortium (USNPC) for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Synthetic Organic Chemical Manufacturers Association (SOCMA) U.S. Nitroglycerin Producers Consortium (USNPC) advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Nitroglycerin

SUMMARY OF COMMENTS

The sponsor, the Synthetic Organic Chemicals Manufacturers Association's U.S. Nitroglycerin Producers Consortium, submitted a test plan and robust summaries to EPA for Nitroglycerin (1,2,3-trinitroglycerin, CAS No. 55-63-0) dated September 25, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 29, 2002.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The data provided by the submitter for physicochemical properties, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program. The submitter needs to provide atmospheric photodegradation information and biodegradation data.

2. Health Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program, except that testing is needed for the chromosomal aberration endpoint. The submitter also needs to address deficiencies in the robust summaries including proper identification of studies.

3. Ecological Effects. All appropriate SIDS-level endpoints have been addressed for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON NITROGLYCERIN CHALLENGE SUBMISSION

Test Plan

Generic Comments

Although the submission cover letter states that all endpoints are addressed, the submitter needs to indicate this explicitly in the test plan.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, water solubility).

The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data provided by the submitter for stability in water and fugacity are adequate for the purposes of the HPV Challenge Program.

Photodegradation. The submitter presented data in the robust summaries on the direct photolysis of nitroglycerin in water. This is insufficient for the purposes of the HPV Challenge Program. The submitter needs to provide data on the atmospheric oxidation and indirect atmospheric photolysis of this chemical.

Biodegradation. The submitter provided two biodegradation studies which suggest that nitroglycerin is

biodegradable. However, both tests provide an environment where an acclimated bacterial population can be developed, which does not provide a conservative estimate of biodegradation (as would an unacclimated population). The submitter needs to provide biodegradation data following OECD Guideline 301 (ready biodegradability), which is performed using an unacclimated population.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, reproductive/developmental toxicity).

EPA agrees with the submitter that adequate data are available for the acute toxicity, repeated-dose toxicity, gene mutation, reproductive and developmental toxicity endpoints. The submitter needs to address deficiencies in the robust summaries and clearly identify the key study supporting each endpoint.

Genetic toxicity: chromosomal aberrations. The studies submitted for *in vivo* chromosomal aberration were not adequate because of the lack of positive controls, the failure to administer the maximum tolerated dose, insufficient numbers of animals for statistical analyses, a lack of information on the sex of test animals, and other deficiencies EPA does not agree that the data in total are sufficient to support a weight-of-the-evidence approach for the chromosomal aberration endpoint. Consequently, testing of nitroglycerin is needed for the chromosome aberration endpoint following the *in vitro* OECD Testing Guideline 473.

Ecological Effects (fish, invertebrates, and algae).

The submitted data are adequate for the purposes of the HPV Challenge Program.

Specific Comments on the Robust Summaries

Generic Comments

The submitter needs to identify the primary citation for each robust summary provided. The information defining the reference should be specific so that the reader can locate the data and examine the details of the study, if necessary. Referencing a database is not adequate identification for data satisfying an HPV endpoint.

Health Effects

Reproductive/Developmental Toxicity. The reproductive parameters specified by the 1966 U.S. FDA guidelines need to be listed in the robust summary for the two-generation reproductive toxicity feeding assay in rats, so that the reader can determine the similarity of the study methods to OECD Guideline 416 from the information provided in the robust summary.

Ecotoxicity

The robust summaries indicated that a base stock solution of 10% nitroglycerin was used in serial dilutions to provide test concentrations for each endpoint. The submitter needs to clarify if the endpoint values provided are for 10 or 100 % active ingredient nitroglycerin.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.